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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,951	05/10/2006	Desuo Wang	16139/09062	5136
27530 7590 05/28/2009 NELSON MULLINS RILEY & SCARBOROUGH, LLP 1320 MAIN STREET, 17TH FLOOR COLUMBIA, SC 29201				
EXAMINER				
STOCKTON, LAURA LYNNE				
ART UNIT		PAPER NUMBER		
1626				
MAIL DATE		DELIVERY MODE		
05/28/2009		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/578,951

Applicant(s)

WANG ET AL.

Examiner

Laura L. Stockton

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on May 10, 2006 (Prelim. Amendment).
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-45 is/are pending in the application.
- 4a) Of the above claim(s) 18-45 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/S508)
Paper No(s)/Mail Date May 10, 2006
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Claims 1-45 are pending in the application.

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-17, drawn to products.

Group II, claim(s) 18-45, drawn to methods of use.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features that

defines a contribution over the prior art. The products claimed contain pyrrolylaminocarbonylmethyl group which does not define a contribution over the prior art. See, for example, the compound of CA Registry No. 760897-03-8. The substituents on the pyrrolylamino-carbonylmethyl group vary extensively and when taken as a whole result in vastly different compounds. Accordingly, unity of invention is considered to be lacking and restriction of the invention in accordance with the rules of unity of invention is considered to be proper.

Additionally, the vastness of the claimed subject matter and the complications in understanding the claimed subject matter imposes a burden on any examination of the claimed subject matter.

During a telephone conversation with

Dr. Marcia Greci on May 20, 2009, a provisional election was made with traverse to prosecute the invention of Group I, claims 1-17 (drawn to products). Affirmation of this election must be made by applicant in replying to this Office action. Claims 18-45 (Group II - drawn to methods of use) are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Restriction for examination purposes as indicated is proper because all these inventions listed in this

action are independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

- (a) the inventions have acquired a separate status in the art in view of their different classification;
- (b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;
- (c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);
- (d) the prior art applicable to one invention would not likely be applicable to another invention;
- (e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined even though the requirement may be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention may be made with or without traverse. To reserve a right to petition, the

election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144.

If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a

nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be

amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Information Disclosure Statement

The Examiner has considered the Information Disclosure Statement filed on May 10, 2006.

Priority

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application).

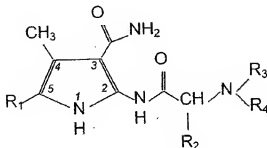
The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/519,140, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

Since the instant application claims the benefit under 35 USC § 119(e) of Provisional application 60/519,140 filed November 12, 2003, the disclosure in the provisional application was reviewed because of the possibility of intervening art. It was found that Provisional application 60/519,140 fails to provide adequate support for the entire scope of the instant claimed invention. See below for the disclosed genus

in Provisional application 60/519,140 which is much smaller genus than the instant claimed products.

The general structure for our invention disclosure is given below. The R groups are inclusively defined, respectively.



where,

R₁=CH₃, CH₂CH₃, CONH₂, CH₂SCH₃, CH₂SCH₂CH₃, CH₂CH₂SCH₃, CH₂CH₂SCH₂CH₃, CH₂NCH₃, CH₂NCH₂CH₃, or the R group of any naturally occurring α-amino acid;

R₂=H, CH₃, CH₂CH₃, CH₂SCH₃, CH₂SCH₂CH₃; CH₂CH₂SCH₃, or CH₂CH₂SCH₂CH₃;

R₃=CH₃, C₂H₅, ηC₃H₇, tC₃H₇, or ηC₄H₉;

R₄=CH₃, C₂H₅, ηC₃H₇, tC₃H₇, or ηC₄H₉.

Therefore, the instant claimed invention can only rely on the filing date of PCT/US04/37813, which is November 12, 2004.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the phrase "A compound having the structure" should be changed to "A compound of the structure".

In claim 1, under the definition of R^5 and R^9 , an "and" is needed before "arylalkyl" for proper Markush language format. See claim 2 for same.

In claim 2, under the definition of R^1 , R^2 and R^3 , it is not possible to have C_1-C_6 alkenyl or C_1-C_6 alkynyl because the minimum number of carbons for these substituents is two. See claims 3-7 for same.

In claims 10 and 11, under the definition of R^2 , the substituents "dimethylthio" and "diethylthio" have valence problems.

In claim 12, the phrase "wherein the compound comprises the structure" should be changed to "wherein the compound is of the structure".

In claim 13, "comprises" should be changed to "is".

In claim 14, the phrase "comprises a dual PDE-4/ Ca^{2+} " is unclear as to its meaning and should be rewritten.

In claim 17, the phrase "comprising a structure described in claim 1" should be changed to "of claim 1".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the

rejections under this section made in this Office
action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 14 and 15 are rejected under 35
U.S.C. 102(a) as being anticipated by CA Registry No.
760897-03-8 (entry date into Registry file on STN is
October 11, 2004).

The compound of CA Registry No. 760897-03-8 is
embraced by the instant claimed invention. Therefore,
the compound of CA Registry No. 760897-03-8 anticipates
the instant claimed invention.

Claims 1-10 and 14-17 are rejected under 35
U.S.C. 102(b) as being anticipated by:

a) **Boehm et al.** {DD 261158} - see, for example, the Compound Number 1 in Table 1 at the bottom of page 2 and Formula III on page 4;

b) **Wang et al.** {Journal of Pharmaceutical Sciences, 1981, 70(6), pages 699-701} - see, for example, Compound IIIId in Table I on page 700;

c) **Sowell et al.** {Journal of Pharmaceutical Sciences, 1981, 70(5), pages 537-541} - see, for example, Compound Vn in Table II on page 539; or

d) **Sowell et al.** {Journal of Pharmaceutical Sciences, 1981, 70(2), pages 135-140} - see, for example, Compound XVI in Scheme II on page 136 and in Table IV on page 139.

Each of the above cited prior art disclose at least one compound that is embraced by the instant claimed invention. Therefore, each of the above cited prior art anticipate the instant claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Wang et al.** {Journal of Pharmaceutical Sciences, 1981, 70(6), pages 699-701}, **Sowell et al.** {Journal of Pharmaceutical Sciences, 1981, 70(5), pages 537-541}, **Sowell et al.** {Journal of Pharmaceutical Sciences, 1981, 70(2), pages 135-140}, **Allen, Jr. et al.** {U.S. Pat. 2,901,489}, **Johnson et al.** {Journal of Pharmaceutical Sciences, 1979, 68(8), pages 955-958} and **Johnson et al.** {Journal of Pharmaceutical Sciences, 1979, 68(3), pages 317-320}, each taken alone.

***Determination of the scope and content of the prior art (MPEP
§2141.01)***

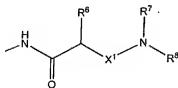
Applicant claims pyrrole compounds. **Wang et al.** (see entire document; particularly page 699; and especially the compounds in Table I on page 700), **Sowell et al. 537** (see entire document; particularly the compounds in Table II on page 539 and the Pharmacology on page 540; and especially Compound Vn in Table II on page 539), **Sowell et al. 135** (see entire document; particularly formula IV on page 135, the compounds in Scheme I and the Pharmacology on page 136; and especially Compound XVI in Scheme II on page 136 and in Table IV on page 139), **Allen, Jr. et al.** (see entire document; particularly the formula in column 1, lines 15-30; and column 2, lines 19-25; and especially Example 1 in column 2 and the first species listed under Example 3 in columns 3-4), **Johnson et al. 955** (see entire document; particularly page 955; and especially Compounds VIIId and VIIIE in Scheme I on page 955) and **Johnson et al. 317** (see entire document;

particularly page 317; and especially Compound VI_f on pages 317 and 319) each teach pyrrole compounds that are either structurally the same as (see above 102 rejection) or structurally similar to the instant claimed compounds.

Ascertainment of the difference between the prior art and the claims
(MPEP §2141.02)

The difference between some of the compounds of Wang et al., Sowell et al. 537 and Sowell et al. 135 and the compounds instantly claimed is that of obvious variances such as homologs.

The difference between the compounds in Allen, Jr. et al. and the compounds instantly claimed is that of positional isomerism (i.e., attachment of the instant



group to the 3-position of the pyrrole ring as found in Allen, Jr. et al. instead of the 2-position of the pyrrole ring as found in the instant claims).

The difference between the compounds found in the Johnson et al. references and the compounds instantly claimed is that of homology (i.e., hydrogen versus lower alkyl at the instant R⁶ variable position as well as various lower alkyls as found in the instant R⁷ and R⁸ variable positions).

***Finding of prima facie obviousness--rational and motivation (MPEP
§2142-2413)***

Position isomers are a basic form of close "structural isomers." MPEP 2144.09, second paragraph, states, "Compounds which are position isomers ... are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties." Nothing unobvious is seen in substituting the known claimed isomer for the structurally similar isomer, as taught by Allen, Jr. et al., since such structurally related compounds suggest one another and would be expected to share common properties absent a showing of unexpected results. In re Norris, 84 USPQ 458 (1950).

Further, it is well established that the substitution of a lower alkyl for a hydrogen atom on a known compound is not a patentable modification absent unexpected or unobvious results. In re Lincoln, 53 U.S.P.Q. 40 (C.C.P.A. 1942), In re Druey, 138 USPQ 39 (C.C.P.A. 1963), In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (i.e., an anti-arrhythmic agent).

One skilled in the art would thus be motivated to prepare positional isomers of the compounds taught in Allen, Jr. et al. or prepare homologs of the compounds taught in the Johnson et al. references to arrive at the instant claimed products with the expectation of obtaining additional beneficial products which would be useful as, for example, an anti-arrhythmic agent.

In terms of the teachings in Wang et al. and both Sowell et al. references, at the very least, such renders at bar obvious as regards these structured compounds and, as regards homologous, isomeric, or other "similar" compounds encompassed in the claims, such are obvious, under 35 U.S.C. § 103 over said reference compounds. In order to establish patentability in adjacent homologs and position isomers, there must at least be a comparative showing establishing distinguishing characteristics allegedly showing that claimed compounds are unobvious. Ex parte Henkel, 130 USPQ 474 (1960). The instant claimed invention would have been suggested to one skilled in the art and therefore, the instant claimed invention would have been obvious to one skilled in the art.

Response to Arguments

Applicant's arguments filed May 10, 2006 have been fully considered but they are not persuasive.

Applicant argues that there is no overlap between the compounds of Johnson et al. 955 and the compounds instantly claimed. Applicant further argues that Johnson et al. 955 fail to provide any suggestion or motivation to produce the presently claimed compounds.

All of Applicant's arguments have been considered but have not been found persuasive. As stated above, Johnson et al. 955 teach pyrrole compounds which are homologs of the compounds instantly claimed. Johnson et al. 955 teach that Compound VIIIe (page 955), for example, was the most active and have activity comparable to lidocaine (page 956, second column). Therefore, Johnson et al. 955 do provide ample motivation to make additional compounds such as homologs.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached on Monday-Friday from 6:00 am to 2:30 pm. If the

examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

The Official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

/Laura L. Stockton/
Laura L. Stockton
Primary Examiner, Art Unit 1626
Work Group 1620
Technology Center 1600

May 27, 2009